SHOULD SURVIVORS OF HEMORRHAGIC STROKES BE RESTARTED ON NOVEL ORAL ANTICOAGULANTS (NOAC)? DEPENDING ON RISK OF RECURRENCE

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The annual risk of suffering from an intracranial haemorrhage (ICH) in patients who are treated with novel oral anticoagulants (NOAC) lies between 0,4% and 0,7% per year according to randomized controlled trials (RCT) that compared the effect of NOACs and warfarin on primary and secondary stroke prevention in patients with atrial fibrillation (AFib).[1-3] The risk of ICH recurrence after starting or restarting NOACs in patients who had suffered from an ICH (spontaneous or in association with antithrombotic treatments) is not known from prospective data. The decision on whether to start or restart NOAC might be based on the balance of two risks: The risk of ischemic stroke if anticoagulation is not restarted and the risk of recurrent ICH if anticoagulation is restarted. For neither of these two risks prospective data exist for patients with an ICH and thus indirect evidence needs to be used.[4]

Factors that predict stroke in patients with AFib are: history of congestive heart failure (CHF), hypertension, age over 75 years, diabetes mellitus, previous stroke, TIA or systemic embolism. These factors are considered by the CHADS-Score, which was used in all NOAC-vs-warfarin trials.[5] Still, most national and international recommendation use the CHA2DS2-VAsc Score which includes some additional aspects: left ventricular dysfunction, pre-existing vascular myocardial infarction, peripheral artery disease, aortic plaques, diabetes mellitus, pre-existing stroke and / or TIA, female gender, and age (> 64 years).[5-7]

Factors that predict the risk of bleeding are summarized in the HASBLED-Score:[8] heart insufficiency, hypertension (systolic blood pressure > 160 mmHg), renal or liver function, pre-existing stroke or TIA, labile INR, age (>65 years), drugs or alcohol. More factors are considered by other bleeding scores but it turned out that the HASBLED performs as well as others while it is easier to use.[9] A post-hoc-analysis of the ICH cases in the trials that compared the prophylactic effect of dabigatran and warfarin in patients with AFib revealed aspirin use, increasing age, and previous stroke or TIA as independent predictors of ICH.[10] The meaning of microangiopathy and microbleeds as predictor of ICH are unclear. Strict blood pressure control seems one prerequisite to prevent recurrence of ICH, since hypertension is a predictor of ICH.[11]

Another concept of risk of recurrence of ICH may be the relation between lesion volume and time after insult: This in known for ischemic stroke where too early start of antithrombotic therapy does increase the risk of haemorrhagic transformation and bleeding with increasing lesion volume and shorter time from onset of stroke. Heidbuchel and colleagues suggested a rule of thumb to assess the bleeding risk depending on lesion size after ischemic infarction.[12] Another piece of information on this concept may be derived from the study by Majeed and co-workers, who looked at the "optimal timing of resumption of warfarin after intracranial hemorrhage".[13] They found out that 2 phases can be differentiated after an ICH that was related to warfarin: An acute phase with a high risk of recurrence of ICH and low risk of ischemic stroke and a post-acute phase were the risk of ICH recurrence becomes lower than the risk of ischemic stroke. The two risks crossed between the 10th and the 30th week after the index ICH. Whether the concept of lesion volume and timing can be transferred to the decision making on restarting anticoagulation after an ICH is unclear and should be subject to further studies.

NOACs per se have a significantly lower risk of ICH when compared with warfarin.[14] This should also be considered in individual case when the decision of restarting anticoagulation after an ICH becomes necessary. Other aspects that may speak for the use of a NOAC over warfarin may be shorter half-life time, fewer drug interactions and easier handling of NOACs. On the other hand treatment measurements are restricted in case of severe NOAC-ICH as there are still no specific antidotes for neither of the NOACs.

Finally, it should be thought of non-pharmacological prevention strategies such as ablation or occlusion of the atrial appendage.[15, 16]

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